

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : C25D 11/36, A61L 27/00 C25D 9/08	A1	(11) International Publication Number: WO 92/13984 (43) International Publication Date: 20 August 1992 (20.08.92)
(21) International Application Number: PCT/CA92/00033 (22) International Filing Date: 31 January 1992 (31.01.92) (30) Priority data: 650,189 4 February 1991 (04.02.91) US (71) Applicant: QUEEN'S UNIVERSITY AT KINGSTON [CA/CA]; Kingston, Ontario K7L 3N6 (CA). (72) Inventor: SHIRKHAZADEH, Morteza ; 64 Ontario Street, Apt. 410, Kingston, Ontario K7L 1X7 (CA). (74) Agent: HICKS, Richard, J.; Intellectual Property, Parteq Innovations, Queen's University, Kingston, Ontario K7L 3N6 (CA).		(81) Designated States: AT (European patent), AU, BE (European patent), BR, CA, CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), JP, LU (European patent), MC (European patent), NL (European patent), SE (European patent). Published <i>With international search report.</i>
(54) Title: METHOD FOR DEPOSITING BIOACTIVE COATINGS ON CONDUCTIVE SUBSTRATES (57) Abstract <p>A process for electro depositing bioactive coatings, such as calcium phosphate or aluminum oxide, onto conductive substrates, such as prosthetic implant devices, is described. An electrolyte bath containing an aqueous solution of the desired oxide or phosphate is prepared with an inert anode such as a platinum anode. A porous or non porous substrate, such as stainless steel or titanium implant is used as the cathode and a D.C. potential is applied so as to raise the interfacial pH at the cathode sufficient to precipitate the desired oxide or phosphate thereon as a dense adherent film.</p>		

FOR THE PURPOSES OF INFORMATION ONLY.

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	FI	Finland	ML	Mali
AU	Australia	FR	France	MN	Mongolia
BB	Barbados	GA	Gabon	MR	Mauritania
BE	Belgium	GB	United Kingdom	MW	Malawi
BF	Burkina Faso	GN	Guinea	NL	Netherlands
BG	Bulgaria	GR	Greece	NO	Norway
BJ	Benin	HU	Hungary	PL	Poland
BR	Brazil	IE	Ireland	RO	Romania
CA	Canada	IT	Italy	RU	Russian Federation
CF	Central African Republic	JP	Japan	SD	Sudan
CG	Congo	KP	Democratic People's Republic of Korea	SE	Sweden
CH	Switzerland	KR	Republic of Korea	SN	Senegal
CI	Côte d'Ivoire	LI	Liechtenstein	SU	Soviet Union
CM	Cameroon	LK	Sri Lanka	TD	Chad
CS	Czechoslovakia	LU	Luxembourg	TG	Togo
DE	Germany	MC	Monaco	US	United States of America
DK	Denmark	MG	Madagascar		
ES	Spain				

Method for Depositing Bioactive Coatings on Conductive
Substrates

Field of Invention

This invention relates to a process for electro deposition of oxide or phosphate coatings onto conductive substrates and the products thereof. More particularly this invention relates to the electro deposition of bioactive coatings such as calcium phosphate onto implantable prosthetic devices and to the coated product.

Background of Invention

It is known that coating prosthetic implant devices such as porous coated orthopaedic prostheses, artificial teeth and the like with an oxide or phosphate coating improves the effectiveness and biocompatibility of the devices, by stimulating bone ingrowth or even bonding chemically to the bone structure. Oxide coatings include alumina and zirconia and phosphate coatings include calcium phosphate (such as α or β tricalcium phosphate Ca_3PO_4 or $\text{Ca}_5(\text{PO}_4)_{3-x}(\text{CO}_3)_x(\text{OH})_{1+x}$ where x is 0.2 or less) and more particularly calcium hydroxyapatite $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$. These coatings are generally of the order of 60 μm thick and it has even been suggested that calcium hydroxyapatite (CHA) coatings on hip implants significantly reduces "mid-thigh

SUBSTITUTE SHEET

pain" in the immediate post operative period. CHA coatings are, therefore, the preferred coating and they are generally applied by plasma spraying or by sol-gel processing methods.

Such application methods are not, however, entirely satisfactory. With plasma spraying, which is a "line-of-sight" process it is extremely difficult, if not impossible, to apply a uniform coating to the irregularly shaped surface of a prosthetic device. Furthermore re-entrant and "back-face" surfaces cannot be coated at all.

With sol-gel processing, it is somewhat easier to coat irregular surfaces but uniformity remains a problem and there is the problem that the coating must be sintered to remove the organic materials and densify the ceramic material. Local overheating of the metallic substrate may affect the physical properties - such as the fatigue and tensile strengths - of the substrate. Electrophoretic deposition of phosphate films onto titanium substrates also suffers from the fact that sintering of the film is required to provide a uniform adherent coating.

Thus, there is a need for an improved process for the deposition of adherent oxide and phosphate bioactive coatings onto conducting substrates of controlled thickness and porosity which do not require substrate heat treatment or sintering.

SUBSTITUTE SHEET

Object of Invention

One object of the present invention is to provide an improved process for the deposition of ceramic coatings, particularly oxide and phosphate coatings on porous and non-porous conducting substrates. Another object of the invention is to provide improved coated products.

Brief Statement of Invention

By one aspect of this invention there is provided a process for electro depositing an adherent ceramic coating on a conducting substrate comprising:

- (a) providing an electrolytic cell having an inert anode and containing an electrolyte comprising an aqueous solution of said ceramic of less than pH8;
- (b) activating said substrate;
- (c) immersing said conducting substrate in said electrolyte;
- (d) applying a DC potential between said anode and said activated substrate so as to raise the pH of said electrolyte at an interface between said electrolyte and said substrate sufficient to precipitate said ceramic onto said activated substrate.

By another aspect of this invention there is provided a conducting substrate having electro deposited thereon an adherent crystalline coating of a ceramic material.

SUBSTITUTE SHEET

Detailed Description of Preferred Embodiments

According to the present invention, a porous or non porous conductive substrate, such as stainless steel, titanium or titanium alloy implantable prostheses, or more particularly knee or hip replacement prostheses are activated by washing in water, and/or grinding or sand-blasting or etching or ultrasonic cleaning and then immersed in an aqueous solution having a pH of less than about 8, i.e. acid or substantially neutral, which contains ions of the ceramic to be deposited and is preferably an acid solution of about pH4 of calcium phosphate tribasic ($\text{Ca}_{10}(\text{OH})_2(\text{PO}_4)_6$) dissolved in hydrochloric acid (about 20g of calcium phosphate/l), as the cathode. Titanium alloys include elements selected from Ta, Nb, Al, V and Pt group metals and combinations thereof. The present invention also contemplates the use of non conducting substrates, such as glass, which are coated with a conducting layer such as Indium Tin Oxide. A platinum anode is also inserted into the solution. A DC potential of between about 0.5 volts and 10 volts and more preferably about 2-3 volts is applied to the electrodes, so as to provide a current density of less than 10 milliamps per sq. cm. The application of a potential cathodically polarizes the substrate and reduces the hydrogen ion concentration at the cathode so that at the surface of the cathode the pH of the solution rises to about pH 8-10

SUBSTITUTE SHEET

and the desired coating such as aluminum oxide and preferably calcium phosphate is precipitated as a dense, adherent film onto the cathode. Adherent coatings of at least 50 μm can be produced at room temperature. As the surface becomes coated with the non conductive coating the electrode becomes progressively more resistive to the passage of the current and the process will eventually stop, thereby limiting the thickness of the film which can be deposited.

Recent evidence indicates that calcium phosphate coatings on prosthetic devices derive their biological activity, in total or in part, by providing a local source of ions essential for bone tissue formation, but immediate incorporation of dissolved Ca and PO_4 ions into bone mineral is not necessarily achieved. Radio-labelled ^{45}Ca experiments show that only a portion of the dissolved ^{45}Ca remains at the implant site, the remainder dilutes the body Ca-pool before incorporation into bone mineral deposits. The effect of increased calcium concentrations is probably not only an effect of mineral precipitation, but also may be a solution-mediated effect on cell proliferation and differentiation. Thus, the density and/or adhesion of the calcium phosphate coatings on the substrate is of secondary importance as the ultimate objective of the present technique is to provide a phosphate coating which will enhance calcified tissue formation within the pores of the metal substrate and the eventu-

SUBSTITUTE SHEET

al bonding of the tissues to the prosthesis occurs through the mechanical interlock between porous metal and bone.

The electrolyte will contain ions to produce the desired ceramic and may contain Ca, P-containing ions and/or Zr^{4+} , Al^{3+} , K^{+} , Na^{+} or ions of platinum group metals and/or other anions such as F^{-} , $CO_3^{=}$, HCO_3^{-} , NO_3^{-} or Cl^{-} , depending upon the desired coating. The electrolyte may also contain organic materials such as proteins and biologically non-toxic compounds such as collagen, plasma fibronectin or impurities. The electrolyte may also contain dissolved oxygen.

As the interfacial pH at the cathode is increased, inorganic ceramic compounds (e.g. Al_2O_3 or calcium phosphate) may co-precipitate with organic compounds. This process also allows doping of specific ions (e.g. $CO_3^{=}$ and F^{-}) in calcium phosphate crystals during the nucleation and crystal growth of calcium phosphate compounds.

A characteristic feature of the present invention is that in coating calcium phosphate compounds on Ti or Ti alloy substrates, the calcium phosphate compound is highly crystalline even when the process is conducted at room temperature. It should be noted that for biocompatibility, crystalline calcium phosphate is preferred to an amorphous calcium phosphate. An amorphous calcium phosphate coating according to the prior art is normally subjected to a high

SUBSTITUTE SHEET

temperature hydrothermal process in order to increase its crystallinity and to improve its biocompatibility. The present process eliminates the need for a hydrothermal step, and therefore organic compounds which may be unstable at high temperatures can be co-precipitated with crystalline calcium phosphate compounds. Another characteristic feature of the present invention is that the calcium phosphate coating is composed of an interlocking network of non-orientated crystals with micro pores and that the coating is firmly adhered to the substrate. The coated substrate therefore provides a large surface area of the calcium phosphate crystals in contact with body fluids when used as an implant. It should be noted that a large surface area of calcium phosphate compound is desirable for better chemical and physical interaction between calcium phosphate compound and the biological environment. The micro pores in the calcium phosphate compound coating also encourage better adhesion of, for example, collagen and other bone macro molecules.

For certain applications however, it is preferred to have a dense calcium phosphate coating on a Ti or Ti alloy substrate. This can be achieved by conducting the process under forced flow conditions where there is a relative velocity between the cathode and the electrolyte. This condition can be provided by, for example, stirring the

SUBSTITUTE SHEET

electrolyte in the cell with a magnetic stirrer or by subjecting the electrolyte to ultrasonic vibrations. Alternatively, the coating can be first applied under stagnant condition (Step 1) and then subjected to ultrasonic vibrations for a short period of time, for example, in a methanol bath to remove the loosely adhered crystals (Step 2). By repeating Steps 1 and 2 several times, a dense and firmly adherent coating of calcium phosphate compound can be achieved even at room temperature. Sintering between 300 and 900°C may also be used to produce a dense coating.

In summary, the nature of the initially precipitated phases and the course of the subsequent crystal growth reaction and crystal morphology is markedly dependent not only upon the degree of saturation and the pH of the electrolyte, but also it is dependent on the applied voltage, ionic strength of the electrolyte, electrolyte temperature, state of the cathode surface, degree of agitation and the types of ions or substance present in the electrolyte. Indeed, the type of phases formed may be influenced by careful control of the physico-chemical conditions.

Example #1

An electrolyte was prepared by adding 20 g calcium phosphate tribasic powder ($\approx \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) (Aldrich Chemical Company, Inc.) and 58.5g sodium chloride (NaCl) to 1 liter of distilled water. The pH of the electrolyte was

SUBSTITUTE SHEET

adjusted to 4.4 by addition of Hydrochloric acid (HCl). The electrolyte was stirred by a magnetic stirrer for 2 hrs to enhance the dissolution of the calcium phosphate tribasic powder. The electrolyte was then filtered through fine sintered glass filters and transferred to a conventional electrolytic cell having a capacity of 1 liter. The cell was fitted with a commercial saturated calomel electrode (SCE) acting as a reference electrode and a platinum foil acting as the anode of the cell. The surface of a Titanium alloy (Ti 6Al 4V) sample 5 cm long, 1 cm wide and 2 mm thick was roughened on both sides by blasting it with a steel grit (Average particle diameter of 0.5 mm) and then cleaned with methanol in an ultrasonic bath for 15 min. The sample was then washed with distilled water and dried in a stream of air. The sample was then immersed in the electrolyte and used as the cathode of the cell.

The cathode, anode and the reference electrode were then connected to a conventional potentiostat operating under potentiostatic condition and the cathode was polarized to -1400 mV with respect to the saturated calomel electrode. No attempt was made to exclude CO₂ from the atmosphere entering the cell. This experiment was conducted at room temperature (T=25°C) for ½ hr and the sample was coated with a layer of calcium phosphate compound.

SUBSTITUTE SHEET.

The sample was then removed from the cell, washed with distilled water and dried in a stream of air for 10 min. Electron microscopic examination of the calcium phosphate coating was carried out using a JEOL-Scanning Electron Microscope (SEM). At relatively high magnification it was observed that the coating had micro pores (pore diameter in the range of 30-50 μm). The coating was composed of an interlocking network of non-oriented plate-like crystals (The average size of crystals was $\approx 20 \mu\text{m}$). The chemical analysis of the coating showed that the coating mainly consisted of a CO_2 -containing calcium phosphate compound with small quantity of Cl, Na and traces of K.

Example #2

An electrolyte identical to the electrolyte in Example #1 was used. A Titanium alloy (Ti 6 Al 4V) sample in the form of a rod having a diameter of 0.5 cm and a length of 10 cm was used as the cathode. The sample had a threaded section at one end having a length of 4 cm. The sample was polarized in a similar manner to Example #1, but at -1300 mV with respect to the saturated calomel electrode. This experiment was run at an electrolyte temperature of 65°C for 2½ hrs. SEM examination of the coated sample revealed that the coating structure comprised an interlocking network of fine and plate-like crystals in the range of 2-5 μm in size. The coating also had fine micro pores of the order of 2-5

SUBSTITUTE SHEET.

μm . The coating was continuous and uniform and firmly adhered to the substrate. The chemical analysis of the coating showed that it mainly consisted of a CO_2 -containing calcium phosphate compound with small amount of Cl. Sodium and potassium were not detectable.

Example #3

An electrolyte identical to that of Example #1 was prepared. A Titanium alloy (Ti 6Al 4V) sample similar to that of Example #2 was used as the cathode. The sample was polarized at -1500 mV (V_{S} SCE) in the electrolyte for $\frac{1}{2}$ hr at 25°C (Step 1). The sample was then removed and subjected to ultrasonic vibration in a methanol bath for 2 min (Step 2). Steps 1 and 2 were repeated alternatively five times. The calcium phosphate coating obtained was fully dense with no porosity. The coating was also continuous, crystalline with very good adhesion to the substrate.

Example #4

An electrolyte identical to that of Example #1 was prepared. A Titanium alloy (Ti 6Al 4V) sample with the same dimensions as in Example #1 was mechanically ground. The sample was coated for $\frac{1}{2}$ hr at -1400 mV (V_{S} SCE), 25°C. The coating was then sintered at 350°C. A fully dense coating of calcium phosphate compound with good adhesion to the substrate was obtained. The coating was uniform and had a

SUBSTITUTE SHEET.

thickness of $\approx 50 \mu\text{m}$. SEM examination showed that the calcium phosphate crystals were sintered together and that the coating was without any pores.

Example #5

Titanium wire having a diameter of 0.3 mm was used to make a three dimensional porous substrate having pores in the range of $500 \mu\text{m}$. An electrolyte similar to that in Example #1 was prepared and the porous substrate was coated according to the procedure used in Example #3. The calcium phosphate coating obtained was uniform, crystalline and was strongly bonded to the porous substrate.

SUBSTITUTE SHEET.

I claim

1. A process for electro depositing an adherent ceramic phosphate coating on a conducting substrate comprising:
 - (a) providing an electrolytic cell having an inert anode and containing an electrolyte comprising an aqueous solution containing ions of said ceramic and having a pH of less than 8;
 - (b) activating said conducting substrate;
 - (c) immersing said conducting substrate in said electrolyte;
 - (d) applying a DC potential between said anode and said activated conducting substrate so as to raise the pH of said electrolyte at an interface between said electrolyte and said activated conducting substrate sufficient to precipitate said ceramic from said electrolyte and onto said activated conducting substrate.
2. A process as claimed in claim 1 wherein said ceramic coating is selected from phosphate coatings and oxide coatings.
3. A process as claimed in claim 2 wherein said phosphate coating is a calcium phosphate compound coating.
4. A process as claimed in claim 3 wherein said phosphaste coating is selected from the group consisting of α and β

SUBSTITUTE SHEET.

tricalcium phosphate and components having a formula $\text{Ca}_5(\text{PO}_4)_{3-x}(\text{CO}_3)_x(\text{OH})_{1+x}$ where x is 0.2 or less.

5. A process as claimed in claim 1 wherein said conducting substrate is selected from stainless steel, titanium and alloys thereof, and a non conducting substrate coated with a conducting layer.

6. A process as claimed in claim 5 wherein said non conducting substrate is glass and said conducting layer thereon is indium-tin oxide.

7. A process as claimed in claim 5 wherein said anode is a platinum anode.

8. A process as claimed in claim 1 wherein said DC potential is in the range of 0.05-10 volts, so as to provide a current density of less than 10 milliamps/sq cm.

9. A process as claimed in claim 5 wherein said conducting substrate is selected from a porous substrate and a non porous substrate.

10. A process as claimed in claim 1 including at least one step selected from the group consisting of (a) conducting said process under forced flow conditions (b) subjecting said coated substrate to ultra sonic vibrations and (c) sintering said coated substrate between 300 and 900°C, so as

SUBSTITUTE SHEET

to produce a densified coating.

11. A process as claimed in claim 1 wherein said electrolyte additionally contains ions selected from fluoride, chloride, carbonate, bicarbonate, nitrate, Pt group metals, and dissolved oxygen and carbon dioxide.

12. A process as claimed in claim 11 wherein said electrolyte additionally contains collagen or organic biologically non-toxic compounds.

13. A conducting substrate having electro deposited thereon an adherent crystalline coating of a ceramic material.

14. A conducting substrate as claimed in claim 13 wherein said ceramic material is a phosphate compound.

15. A conducting substrate as claimed in claim 14 wherein said oxide is selected from alumina and zirconia.

16. A conducting substrate as claimed in claim 14 wherein said phosphate is a calcium phosphate compound.

17. A conducting substrate as claimed in claim 13 wherein said substrate is a porous metallic substrate.

18. A conducting substrate as claimed in claim 17 wherein said metallic substrate is selected from stainless steel, titanium and titanium alloys.

SUBSTITUTE SHEET

19. A conducting substrate as claimed in claim 13 wherein said substrate is a non conducting substrate coated with a conducting layer.
20. A conducting substrate as claimed in claim 19 wherein said non conducting substrate is glass and said conducting layer is indium tin oxide.
21. A biologically inactive metallic implant prosthetic device having electro deposited on at least one selected surface thereof an adherent layer of a bioactive, ceramic material selected from an oxide coating and a phosphate coating.
22. A prosthetic device as claimed in claim 21 wherein said metallic implant is selected from stainless steel, titanium and titanium alloys.
23. A prosthetic device as claimed in claim 22 wherein said adherent layer is a micro porous crystalline layer.
24. A prosthetic device as claimed in claim 22 wherein said adherent layer includes a calcium phosphate compound coating doped with at least one ion selected from, CO_3 , F, Cl, K, Na, and Pt group.
25. A prosthetic device as claimed in claim 21 wherein said coating comprises calcium phosphate compound co-precipitated

SUBSTITUTE SHEET.

with at least one of alumina and zirconia.

26. A prosthetic device as claimed in claim 22 wherein said adherent layer comprises calcium phosphate compound co-precipitated with at least one biologically active compound selected from the group consisting of collagen and plasma fibronectin.

SUBSTITUTE SHEET

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 92/00033

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC Int.Cl. 5 C25D11/36; A61L27/00; C25D9/08		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification Systems	Classification Symbols	
Int.Cl. 5	C25D ; A61L	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category ¹⁰	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	FR,A,2 262 134 (SOCIETE CONTINENTALE PARKER) 19 September 1975 see page 2, line 17 see page 3, line 7 - line 32 ---	1,2,3,5, 7,8,9, 11,13, 14,16, 17,18
X	PATENT ABSTRACTS OF JAPAN vol. 11, no. 242 (C-438)(2689) 7 August 1987 & JP,A,62 050 496 (NIPPON KOKAN KK) 5 March 1987 see abstract --- -/--	1,2,3,5, 7,8,9, 11,14, 16,17,18
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>¹⁰ Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
23 APRIL 1992	19.05.92	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE	NGUYEN THE NGHIEP N.	

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
X	CHEMICAL ABSTRACTS, vol. 80, no. 20, . 20 May 1974, Columbus, Ohio, US; abstract no. 115498N, MATSUSHIMA: 'cathodic treatment of metal surfaces' page 511 ; see abstract	1,2,3,5, 7,8,9, 11,14, 16,17,18
A	EP,A,0 232 791 (TECHNISCHE HOCHSCHULE KARL - MARX - STADT) 19 August 1987	

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO. CA 9200033
SA 55850**

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information. 23/04/92

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR-A-2262134	19-09-75	JP-C- 1042742	23-04-81
		JP-A- 50115138	09-09-75
		JP-B- 54029979	27-09-79
		DE-A- 2505836	04-09-75

EP-A-0232791	19-08-87	JP-A- 62204760	09-09-87
		US-A- 4846837	11-07-89

EPO FORM PCT/89

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82